

Enjaymo® (Sutimlimab-Jome) (for Ohio Only)

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Related Policies
None

Application

This Medical Benefit Drug Policy only applies to the state of Ohio. Any requests for services that are stated as unproven or services for which there is a coverage or quantity limit will be evaluated for medical necessity using Ohio Administrative Code 5160-1-01.

Coverage Rationale

Enjaymo® is medically necessary for the treatment of cold agglutinin disease (CAD) in patients who meet all of the following criteria:

- For **initial therapy**, all of the following:
 - Diagnosis of CAD by, or in consultation with, a hematologist with expertise in the diagnosis of CAD; **and**
 - Confirmation of the CAD diagnosis based on **all** of the following:
 - Evidence of chronic hemolysis [e.g., elevated lactated dehydrogenase (LDH), decreased haptoglobin, increased indirect bilirubin, increased reticulocyte count]; **and**
 - Positive polyspecific direct antiglobin test (DAT); **and**
 - Positive monospecific DAT specific for C3d; **and**
 - Immunoglobulin G (IgG) DAT ≤ 1+; **and**
 - Cold agglutinin titer ≥ 64 at 4°C
 - and**
 - Cold agglutinin syndrome secondary to other factors has been ruled out (e.g., infection, rheumatologic disease, systemic lupus erythematosus, overt hematologic malignancy, other autoimmune disorders); **and**
 - Patient has a baseline hemoglobin level ≤ 10 g/dL; **and**
 - Enjaymo® is prescribed by a hematologist; **and**
 - Enjaymo® dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
 - Patient is not receiving Enjaymo® in combination with a complement inhibitor [e.g., Soliris (eculizumab), Ultomiris (ravilizumab-cwzb), Empaveli (pegcetacoplan), Fabhalta (iptacopan), PiaSky (crovalimab), Zilbrysq (zilucoplan)]; **and**
 - Initial authorization will be for no more than 12 months
- For **continuation of therapy**, all of the following:
 - Documentation of positive clinical response to therapy (e.g., increase in hemoglobin, decreased transfusion requirements, decreased markers of hemolysis, improvement in anemia-related symptoms); **and**
 - Enjaymo® is prescribed by, or in consultation with, a hematologist; **and**
 - Enjaymo® dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**

- Patient is not receiving Enjaymo® in combination with a complement inhibitor [e.g., Soliris (eculizumab), Ultomiris (ravilizumab-cwzb), Empaveli (pegcetacoplan), Fabhalta (iptacopan), PiaSky (crovalimab), Zilbrysq (zilucoplan)]; **and**
- Reauthorization will be for no more than 12 months

Requests outside of this criteria will be reviewed for medical necessity on a case-by-case basis.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state, or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
J1302	Injection, sutimlimab-jome, 10 mg

Diagnosis Code	Description
D59.12	Cold autoimmune hemolytic anemia

Background

Cold agglutinin disease (CAD) is a form of autoimmune hemolytic anemia (AIHA) in which cold agglutinins can cause clinical symptoms related to agglutination of red blood cells in cooler parts of the body and hemolytic anemia. Primary chronic cold (hem)agglutinin disease accounts for about 15-25% of AIHAs. CAD is defined as an AIHA mediated by cold agglutinins (CAs), without any obvious underlying disease such as aggressive lymphoma, other overt malignancies, or specific infections. CAs are autoantibodies that are able to agglutinate red blood cells (RBCs) at an optimum temperature of 3-4°C, but can also react at higher temperatures, depending on the thermal amplitude.

Hemolysis in CAD is primarily extravascular and mediated by complement. The IgM cold agglutinin binds to an antigen on the surface of RBCs in sites of the body where the temperature is low enough to be in the thermal range of the antibody. The bound IgM recruits components of the classical pathway of complement, such as C1, C4, and C2. C1-esterase activates C4 and C2, leading to production of the C3 convertase, which cleaves C3 to C3a and C3b. Lastly, C3b-coated RBCs undergo extravascular hemolysis due to phagocytosis by macrophages in the liver.

Clinical Evidence

An International Consensus Group published recommendations in 2019 on the diagnostic and therapeutic approach for autoimmune hemolytic anemias, including cold agglutinin disease (CAD). Diagnostic recommendations for CAD include markers of chronic hemolysis accompanied by a direct antiglobin test (DAT, direct “Coombs test”) for C3d, with a cold agglutinin (CA) titer of 64 or greater at 4°C. Treatment recommendations included watchful waiting in patients with hemoglobin levels > 10 g/dL unless comorbid ischemic cardiac disease or chronic obstructive pulmonary disease was present with blood transfusions recommended when indicated. Recommended treatment goals included improvement in hemoglobin levels and improvement in symptoms. Rituximab monotherapy was a recommended first-line therapy for those requiring chronic treatment as response rates of 50% have been reported in uncontrolled trials. Alternative first and second-line recommendations include rituximab combined with bendamustine or fludarabine. A 71% response rate has been reported with rituximab plus bendamustine combination therapy, with 40% achieving complete response (CR) and 31% partial response (PR). Hemoglobin levels increased by a median of 4.4 g/dL in the complete responders and 3.9 g/dL in those who had a PR. Median time to response was 1.9 months, and less than 10% of the responders had relapsed at 32 months. A 76% response rate has been reported with rituximab plus fludarabine combination therapy, with 21% achieving CR and 55% achieving PR. Median increase in Hb level was 3.1 g/dL in the responders and 4.0 g/dL among those who achieved CR. Median time to response was 4.0 months, and estimated median response duration was more than 66 months.

Sutimlimab was studied in a 26-week open-label, single-arm, multicenter phase 3 CARDINAL study (Part A) with a 2-year extension phase (Part B). Patients with a confirmed diagnosis of CAD based on chronic hemolysis, polyspecific DAT, monospecific DAT specific for C3d, cold agglutinin titer ≥ 64 at 4°C, and IgG DAT ≤ 1 + were enrolled. Eligibility criteria

included baseline hemoglobin (Hb) \leq 10 g/dL, total bilirubin level above normal, and \geq 1 blood transfusion in the prior 6 months. Sutimlimab was administered intravenously on Days 0 and 7, followed by biweekly infusions. Patients weighing $<$ 75 kg or \geq 75 kg received a 6.5 g or 7.5 g dose, respectively. The primary efficacy endpoint was response rate based on a composite of Hb increase \geq 2 g/dL or Hb \geq 12 g/dL at treatment assessment and transfusion avoidance from Weeks 5 to 26. Secondary efficacy endpoints included change from baseline in hemolytic markers (e.g., bilirubin) and quality of life (QOL) measured by the Functional Assessment of Chronic Illness Therapy Fatigue (FACIT-F) Scale.

Twenty-four patients enrolled and received \geq 1 dose of sutimlimab. The mean (standard deviation) age was 71.3 (8.2) years with 62.5% females. Mean (range) baseline Hb was 8.6 (4.9 -11.1) g/dL. The median (range) number of transfusions within 6 months prior to enrollment was 2 (1-19) and 62.5% of patients had failed prior therapies. Out of 24 patients, 22 completed Part A; 2 patients were withdrawn early for reasons unrelated to the study drug. The prespecified primary endpoint was met in 13 (54.2%) patients. The estimated mean Hb increase at treatment assessment time point was 3.2 g/dL. Hb improved rapidly after the first dose of sutimlimab with 1.2 g/dL and 2.3 g/dL increases by Weeks 1 and 3, respectively. Mean overall Hb was maintained above 11 g/dL after Week 3. Twenty (83.3%) patients had a Hb increase \geq 1 g/dL. Fifteen (63%) patients had a Hb increase \geq 2 g/dL. Nine (38%) of patients had a Hb level of \geq 12 g/dL. Mean total bilirubin was normalized by Week 3. Seventeen (70.8%) patients remained free of transfusions from Weeks 5 to 26. FACIT-F scores improved within 1 week, peaking by Week 5, and remained stable through Week 26.

Interim results of the Part B extension phase have been reported at 1-year follow-up. The primary objectives of the interim Part B analysis are to evaluate long-term safety and tolerability of sutimlimab for \geq 53 weeks; secondary objectives are to investigate the durability of response over time. Efficacy endpoints included change from baseline in hemolytic markers and the patient-reported outcome: Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) Scale. All patients who completed Part A entered Part B. Hb improved rapidly after first sutimlimab dose and mean Hb was $>$ 11 g/dL from Week 5 to Week 53. Mean total bilirubin was normalized by Week 3 and remained $<$ 20 μ mol/L to Week 53. Normalization of mean absolute reticulocyte count was observed alongside normalized haptoglobin levels and reductions in lactate dehydrogenase. Seventeen (70.8%) and 19 (86.4%) patients remained transfusion-free from Week 5 to Week 26 and Week 26 to Week 53, respectively. From baseline to Week 53, all 24 patients experienced \geq 1 treatment-emergent adverse event (TEAE); 12 (50.0%) patients experienced a serious TEAE. One serious TEAE (viral infection) was associated with sutimlimab. Serious (including bacterial) infections were reported, but no meningococcal infections were identified. There was 1 TEAE of device-related thrombosis (assessed as unrelated to study drug) in Part B; there were no other vascular thromboembolic TEAEs. One patient died due to a progressive carcinoma (unrelated to study drug).

The efficacy of sutimlimab was assessed in a 6-month placebo-controlled CADENZA trial in 42 patients. Following the completion of the 6-month treatment period (Part A) in which 22 patients received sutimlimab and 20 patients received placebo, 39 patients (19 patients on sutimlimab and 20 patients on placebo) continued to receive sutimlimab in a long-term safety and durability of response extension phase (Part B) for an additional 12 months following last patient out from Part A. The trial included a 9-week safety follow-up after the last dose of sutimlimab. Patients with a confirmed diagnosis of CAD based on chronic hemolysis, polyspecific direct antiglobulin test (DAT), monospecific DAT specific for C3d, cold agglutinin titer \geq 64 at 4°C, an IgG DAT \leq 1+ and no history of transfusion within 6 months, or more than one blood transfusion in the 12 months prior to enrollment in the trial. Efficacy was based on the proportion of patients (responders) who met the following criteria: an increase from baseline in hemoglobin level \geq 1.5 g/dL at the treatment assessment time point (mean value from weeks 23, 25, and 26), no blood transfusion from week 5 through week 26, and no treatment for CAD beyond what was permitted per protocol from week 5 through week 26. The responder rate was 72.7% with Enjaymo[®] and 15% with placebo (treatment difference 58.78, 95% CI: 34.6, 82.96; $p = 0.0004$). The most common adverse reactions (\geq 18%) were rhinitis, headache, hypertension, acrocyanosis, and Raynaud's phenomenon.

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Enjaymo[®] is a classical complement inhibitor indicated for the treatment of hemolysis in adults with cold agglutinin disease (CAD).

References

1. Enjaymo[®] [package insert]. Waltham, MA: Bioverativ USA Inc.; February 2024.
2. Jäger U, Barcellini W, Broome CM, et al. Diagnosis and treatment of autoimmune hemolytic anemia in adults: Recommendations from the First International Consensus Meeting. *Blood Rev.* 2020. May;41:100648.
3. Berentsen S. Cold agglutinin disease. *Hematology Am Soc Hematol Educ Program.* 2016. Dec 2;2016(1):226-231.

4. Berentsen S. New Insights in the Pathogenesis and Therapy of Cold Agglutinin-Mediated Autoimmune Hemolytic Anemia. *Front Immunol.* 2020. Apr 7;11:590.
5. Brugnara C, Berentsen S. Cold agglutinin disease. In: UpToDate, Brodsky RA, Tirnauer JS, (Ed), Wolters Kluwer. (Accessed on February 10, 2025).
6. Roth A, Barcellini W, D'Sa S, et al. Inhibition of Complement C1s with Sutimlimab in Patients with Cold Agglutinin Disease (CAD): Results from the Phase 3 Cardinal Study. *Blood.* 2019. 134 (Supplement_2): LBA-2. <https://doi.org/10.1182/blood-2019-132490>.
7. Roth A, Barcellini W, D'Sa S, et al. Inhibition of Complement C1s with Sutimlimab in Patients with Cold Agglutinin Disease (CAD): Interim Results of the Phase 3 Cardinal Study Long-Term Follow-up. *Blood.* 2020. 136 (Supplement 1): 24–25. <https://doi.org/10.1182/blood-2020-138909>.
8. A Study to Assess the Efficacy and Safety of BIVV009 (Sutimlimab) in Participants With Primary Cold Agglutinin Disease Who Have a Recent History of Blood Transfusion (Cardinal Study). *Clinicaltrials.gov* website <https://clinicaltrials.gov/ct2/show/NCT03347396?term=sutimlimab&draw=2&rank=1>.
9. Roth A, Barcellini W, D'Sa S, et al. Sutimlimab in Cold Agglutinin Disease. *N Engl J Med.* 2021;384(14):1323-1334.
10. Berentsen S. How I manage patients with cold agglutinin disease. *Br J Haematol.* 2018;181(3):320-330.
11. Hill QA, Stamps R, Massey E, et al. The diagnosis and management of primary autoimmune haemolytic anaemia. *Br J Haematol.* 2017;176(3):395-411.
12. Berentsen S. How I treat cold agglutinin disease. *Blood.* 2021;137(10):1295-1303.

Policy History/Revision Information

Date	Summary of Changes
06/01/2025	<p>Coverage Rationale</p> <ul style="list-style-type: none"> ● Updated list of examples of complement inhibitors the patient must not be receiving in combination with Enjaymo; added PiaSky (crovalimab) <p>Supporting Information</p> <ul style="list-style-type: none"> ● Updated <i>References</i> section to reflect the most current information ● Archived previous policy version CSOH2024D0100.B

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state (Ohio Administrative Code [OAC]), or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state (OAC), or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state (OAC), or contractual requirements for benefit plan coverage govern. Before using this policy, please check the federal, state (OAC), or contractual requirements for benefit plan coverage. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the InterQual[®] criteria, to assist us in administering health benefits. The UnitedHealthcare Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.